

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) *20 AUG 2005* see form PCT/ISA/210 (second sheet)

X15439

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/035513

International filing date (day/month/year)
08.11.2004

Priority date (day/month/year)
20.11.2003

International Patent Classification (IPC) or both national classification and IPC
C07C311/08, C07C311/09, C07C309/66, C07C309/65, A61K31/255, A61K31/18, A61P19/08, A61P19/10

Applicant
ELI LILLY AND COMPANY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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10/577967

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/035513

IAP20 Rec'd PCT/PTO 02 MAY 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/035513

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 21-26,30-32

because:

☒ the said international application, or the said claims Nos. 21-26 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 30-32 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/035513

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-29
	No: Claims	
Inventive step (IS)	Yes: Claims	1-29
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-20,27-29
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

PCT/US2004/035513

Re Item III**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. For the assessment of the present claims 21-26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
2. Claims 30-32 are considered to be so lacking in clarity that no opinion can be given on these claims (Art. 6 PCT). The reason is that these claims contain no technical features but refer rather in a general fashion to the description. Therefore no examination as to novelty or inventive step of these claims has been performed.

Re Item V**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

3. Reference is made to the following document:
D1 = US-A-6 218 430
D2 = J.A.C.S
D3 = Bioorg. & Med. Chem.
D4 = WO-2004/063345
D5 = WO-2004/048309
4. The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses the use of compounds having a basic bisphenylmethane structure to be useful as vitamin D₃ mimetic.
5. The presently claimed compounds differ from those of D1 especially in the choice of the substituents R_C which is a sulphonic acid ester or sulphonic acid amide. Although

similar sulphonic esters are known from the documents D2 and D3 these documents do not disclose compounds falling under the general definition given in claim 1. As such the presently claimed subject-matter can be considered to satisfy the requirements of Art. 33 (2) PCT with respect to D1.

6. The problem to be solved by the present invention may therefore be regarded as providing alternative compounds for use as vitamin D₃ mimetic.
7. The solution proposed in claim 1 of the present application can be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.
In the document D1 compounds are disclosed in which the group corresponding to R_C is either a carboxylic acid ester or amide. The compounds disclosed in 2 and D3 are not indicated to have a vitamin D mimetic activity. There is no indication in the prior art from which the skilled man could have expected that the claimed compounds would display the desired D₃-mimetic properties. The compounds of claim 1 are considered to present none obvious alternatives to the compounds known from D1.
8. The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding claims 2-15 (which are in fact claims towards preferred compounds according to claim 1), which therefore are also considered to satisfy the requirements of Art. 33 (2) and 33 (3) PCT.
9. Claims 16-20 are claims towards (pharmaceutical) compositions and claims 27-29 are compounds for use a medicaments comprising a compound according to claim 1. As such these claims can also be considered to satisfy Art. 33 (2) and (3) PCT.

Re Item VI Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-2004/063345	29.07.2004	07.01.2004	10.01.2003
WO-2004/048309	10.06.2004	20.11.2003	22.11.2002

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/035513

The documents D4 and D5 both carry publication dates which lie between the priority date and the filing date of the present application. The priority of the present application has not been checked. The documents D2 and D3 could be relevant for the present application if the priority were found not to be valid.